

## Review Article

# Thiomers: A Blessing to Evaluating Era of Pharmaceuticals

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Thiomers are the polymers modified for the mucoadhesive properties and other additive properties by incorporating thiol moieties in the backbone of the unmodified polymeric chain by substitution reactions or simple oxidation reactions. Drugs that are less soluble and permeable can be complexed with thiomers for their increased absorption through the mucosal membranes by increase in contact time and prolonged stay in body due to mucoadhesion. Immobilization of thiol group therefore increases the mucoadhesive properties of the modified polymer by 2–140-folds. The prepared thiomers are characterized and made stable by different techniques. Thiomers also give the controlled delivery of the active pharmaceutical ingredients in the body. Different polymers that are modified by thiolation are chitosan, polyacrylic acid, sodium alginate, sodium carboxy methyl cellulose, guar gum, and so forth. Thiomeric formulations are a challenge to deliver drugs with low therapeutic compatibility. Micro- and nanopreparations containing thiomers can be prepared by different techniques such as covalent crosslinking, in situ gelation, radical emulsion polymerization, and emulsification. Nowadays thiomers have wide range of applications as a promising pharmaceutical excipient in the evaluating era of pharmaceutical technology.

## 1. Introduction

Bioadhesion is the phenomenon by which any molecule adheres to the biological membrane but when the adherence to the mucus is specified it is referred to as mucoadhesion [1]. Mucoadhesion is introduced in the pharmaceutical field for more than 40 years and it is of main importance in oral delivery systems, as drugs taken from oral route have various bioavailability issues [2, 3]. Adhesion to the membranes is of importance as it prolongs the stay of the drug in the body subsequently increasing bioavailability of the drug which in turn improves patient compliance [4]. The natural or synthetic macromolecules are present that adhere to the mucus layer by interacting with the glycoproteins in the mucus, not by covalent bonding, but by weak ionic interactions such as hydrogen bonding and van der Waal's forces [1, 5]. Nowadays, efforts are being made to increase the mucoadhesive properties of the polymer such as improved resistance to enzymes, increased cohesive force and facilitated paracellular diffusion of the drug, increased bioavailability,

and increased patient compliance [2, 6]. For this purpose, the new generation of mucoadhesive polymers developed by integrating sulfhydryl groups on the backbone of the polymer resulted in thiolated polymers, also called as thiomers [6, 7]. This structural modification in the polymer has led to the improvement in the mucoadhesive properties of the polymers by 2- to 140-fold [8]. Polymers modified are

- (i) alginate,
- (ii) chitosan [2],
- (iii) polycarbophil [9],
- (iv) polyacrylic acid [1],
- (v) xyloglucan [5],
- (vi) carboxy methyl cellulose [10],
- (vii) polyaspartamide [11, 12],
- (viii) hydroxyethyl cellulose [13].

TABLE 1: Examples of cationic and anionic polymers.

Cationic thiomers	Anionic thiomers
Hydroxyethyl cellulose	Polyacrylic acid cystamine conjugate
	Sodium carboxy methyl starch (CMS)
	Carboxy methyl guar gum (CMG)
	Carboxymethyl cellulose
	Sodium alginate
Chitosan	

## 2. Types of Thiomers

Followings are the types of thiomers:

- (i) *Cationic thiomers.*
- (ii) *Anionic thiomers.*

**2.1. Cationic Thiomer.** Basically these are the thiomers based on chitosan, prepared by immobilizing thiol group on 2-amino position of the glucosamine, present in the polymer chain. Examples include chitosan cysteine, chitosan-thioglycolic acid, chitosan-thio butyl amidine, and so on (Table 1) [2].

**2.1.1. Chitosan.** Chitosan, a natural mucoadhesive polysaccharide polymer, obtained from deacetylation of chitin present in the crustacean shell, is chemically named as [poly {(1, 4)-2-amino-2-deoxy-d-glucopyranose}]. It consists of two subunits N-acetylglucosamine and glucosamine [14]. Chitosan has the mucoadhesive and permeation enhancing properties due to interaction of the amino group with the anionic structures in the mucus or epithelial layer due to its polycationic nature [15]. The primary amino group present in glucosamine is easily protonated in acidic media which increases its solubility, while it remains stable in basic and neutral media [2, 16].

Modified generation of chitosan is prepared with more pronounced mucoadhesive properties by incorporating thiol group on the backbone of the polymer that is creating the thiolated chitosan [17]. Thiolated chitosan is with improved mucoadhesive properties, enhanced permeation, and in situ gelling properties such as chitosan thio butyl amidine conjugate, chitosan cysteine conjugate, and chitosan thioglycolic acid conjugate [2, 18].

**2.1.2. Increased Mucoadhesive Property of Chitosan.** Thiolated chitosan is the modified polymer having ability to bind with the mucin through covalent bonding rather than weak ionic interactions such as hydrogen bonding or van der Waal's forces as simple chitosan. Sulphur present in the thiolated chitosan makes disulfide bonding with the cysteine rich domain of the mucin thus increasing time to stay in body which in turn increases bioavailability and also may help to reduce dosing frequency which ultimately increases patient compliance [2].

**2.1.3. Mucin.** Mucin is a glycoprotein consisting of protein core with branched oligosaccharides over 63% of its length

and makes 5% of total mucus. It accounts for gel like properties of the mucus. Cysteine present in the mucin glycoprotein accounts for 1.5% of the amino acid in the small intestine that is about 9  $\mu\text{mol SH/g}$  of mucus [2].

**2.1.4. Preparation of Thiolated Chitosan.** Thiolated chitosan is prepared by introducing the sulfhydryl bearing moiety on the 2-amino position of the glucosamine subunit. This is done by reacting carboxylic group of the moiety such as cysteine or thioglycolic acid with the amino group in the polymer backbone leading to formation of the amide bond or amidine bond, in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDAC) or thiobutyric acid, respectively, as coupling agent. Thiol group may undergo oxidation so synthesis must be done under inert conditions or at  $\text{pH} < 5$ , as at this pH the concentration of the thiol anions is low so disulfide formation seldom occurs [2, 4, 19].

The schemes of reactions involved in the formation of thiolated chitosan are shown in Figure 1. It shows two schemes indicating one step process and two-step process. Single step processing of chitosan to achieve thiolated chitosan shows reaction medium consisting of water. The thiolation takes place in the presence of carbodiimide (EDAC) and NHS (N-hydroxysuccinimide). While the second process involves the two steps, first step involves DMF (N,N-dimethylformamide) as a reaction medium to avoid hydrolysis of the ester formed thereby in the reaction. This scheme is shown in Figure 1 [16].

**2.1.5. Degree of Effective Thiol Immobilization.** Studies have shown that immobilization of 25–250  $\mu\text{mol}$  thiol groups per gram of the chitosan is effective in improving the mucoadhesive properties [20] and permeability of the chitosan polymer. If the thiol groups are reduced their immobilization can be determined by Ellman's reagent, while if they are oxidized then by borohydride. Alternatively iodine titration method can be used [4].

**2.1.6. Effect on Mucoadhesion.** Mucoadhesive properties of the chitosan are enhanced by 5–10-fold in case of thioglycolic acid conjugate and 10–20-fold in case of chitosan-4-thiobutylamidine conjugate [2, 21]. The main perspective of thiolation is to increase the mucoadhesion. Mucoadhesion of different polymers increase by many folds with the addition of thiol group (Table 2) [22, 23].

**2.1.7. Mechanism of Mucoadhesion of Thiomers [2].** Mucin is present all over the mucus membrane which has cysteine rich domains. The thiol group interact with these cysteines and lead to formation of the disulfide bonds either by oxidation of the thiol groups or by thiol/disulfide exchange reaction (Figure 2).

The extent to which the mucoadhesion takes place depends upon the pKa of the thiol group, pH of thiolated chitosan, and pH of the surrounding medium. The disulfide bonds thus formed are not influenced by the ionic strength and pH condition.

**2.1.8. In Situ Gelling of Chitosan [24].** Ability of chitosan to crosslink adds more to its mucoadhesive efficiency. For

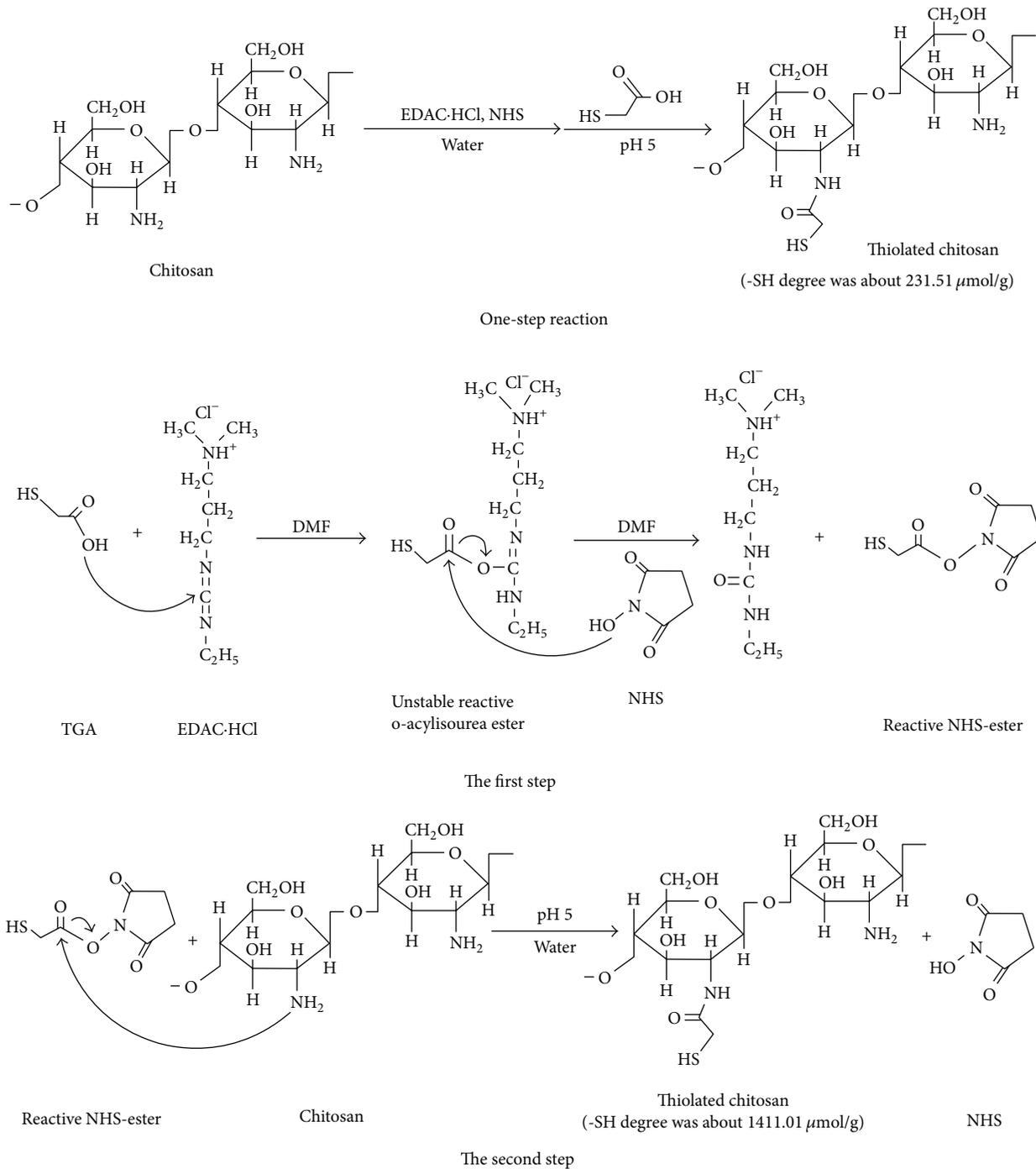


FIGURE 1: Process for thiolation of chitosan.

the chitosan, after forming surface interaction, it starts to form bonds with itself leading to more strong adhesion. The in situ gelling property of chitosan has been of great value for nasal, vaginal, and other preparations [2].

Thiolated chitosan has shown more pronounced gelling property in comparison to unmodified chitosan. The thiol groups interact with each other leading to formation of more strong gel. This occurs due to oxidation of the thiol group

at physiological pH. At pH 5.5, the sol gel transition of the thiolated chitosan occurs after 2 h. When the thiolated chitosan is rheologically observed for the gelling property, it has shown significant decline in the thiol group concentration showing formation of disulfide bond formation. Also, thiolated chitosan shows more elasticity in comparison. The in situ gel forming property of thiolated chitosan is important in case of liquid or semisolid preparation for nasal, vaginal,

TABLE 2: Thiomers with their effect on mucoadhesion [11].

Thiomer	Increase in mucoadhesive strength
Chitosan iminothiolane	250 times
Polyacrylic acid-cysteine	100 times
Polyacrylic acid-homocysteine	Approx. 20 times [21]
Chitosan thioglycolic acid	10 times
Chitosan-thioethylamidine	9 times
Alginate cysteine	4 times
Poly methacrylic acid-cysteine	Improved cohesiveness and mucoadhesion [42, 43]
Sodium carboxy methyl cellulose-cysteine	Increased mucoadhesion
Gellan gum-2-iminothiolane	Increased mucoadhesion [44]
Carbopol 980	Increased mucoadhesion [45]
Hyaluronic acid-L-cysteine	Increased mucoadhesion [46]
Carboxymethyl hyaluronic acid	Improved cohesiveness and mucoadhesion [47]
Poly(ethylene glycol)-glutathione	Improved drug delivery [48, 49]
Sodium alginate	Improved drug delivery [27]

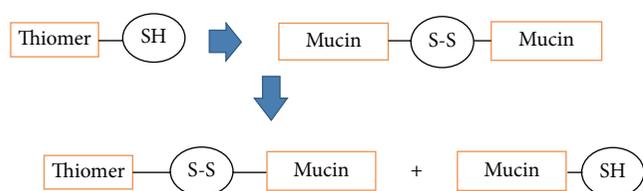


FIGURE 2: Mechanism of mucoadhesion of thiomers.

or ocular use, where thin layer of solution is applied which forms gel layer on mucus and thereby increases the contact time and thus bioavailability of the drug in the body [2].

**2.1.9. Effect on Permeation.** Thiolation of chitosan enhances its permeation effect many folds as compared to the simple chitosan. It can be assayed by using Ussing chamber, through the fresh intestinal mucosa. The studies have shown increase in the uptake of fluorescent bacitracin by 1.6-fold using chitosan cysteine, while, for cysteine-TBA it has shown increase of cationic marker rhodamine 123 uptake by 3-fold as compared to unmodified chitosan [2].

**2.1.10. Mechanism of Permeation Enhancement.** Permeation enhancement effect of the thiolated chitosan can be explained by its effect on protein tyrosine phosphatase, the enzyme that is responsible for dephosphorylation of the transmembrane occludin tyrosine, the protein responsible for opening and closing of these tight junctions between cells. Thiolated chitosan inhibits this dephosphorylation to increase the permeation for drug, thus increasing bioavailability [2].

#### 2.1.11. Thiolated Chitosan in Different Dosage Forms

**Microparticles.** Microparticulate dosage forms due to their small size have the ability to increase the bioavailability due to their increased time to stay in the body. Now when thiolated chitosan with improved mucoadhesive property and being

more resistant to degradation is incorporated, the dosage form with more pronounced properties will be obtained [2]. Microparticles of thiolated polycarbophil were also prepared and shown to have 3-fold mucoadhesion as compared to unmodified polycarbophil [25].

**Tablets.** 40% of all formulations are tablets. Thiolated chitosan can be incorporated for the prolonged release effect to the dosage form due to its in situ gelling properties. If only drug is mixed with polymer and compressed into tablet, it can still show zero order release for several hours. It shows hydration and diffusion account for the release rate [2].

**Solutions.** Thiolated chitosan seems to be unstable when in solution form due to its gelling property and disulphide bond formation within the polymer. This polymer used in solution formulations for eye can be effective in the most common eye problem, dry eye, the condition in which mucous layer of eye acting as a surfactant becomes defective, and there it can be used to form protective layer to cope with this condition [2].

**Gels.** Thiolated chitosan gel formulation seems to be very effective as compared to simple chitosan gels due to the thiolated backbone which enhance its mucoadhesive properties [2].

**2.1.12. Hydroxyethyl Cellulose.** Hydroxyethyl cellulose-cysteamine is synthesized by open ring oxidative amination of the hydroxyethyl cellulose to incorporate thiol groups on the polymer chain. The modified polymer thus obtained has 3-fold more viscosity in comparison to the unmodified hydroxyethyl cellulose. Also the swelling properties and the mucoadhesion are markedly improved [16, 26].

**2.2. Anionic Thiomer.** Carboxylic acid group is present as the substrate in anionic thiomers. Presence of carboxylic groups makes the immobilization of the thiol groups to these polymers more efficient by amide bond formation in the presence of carbodiimides. Examples include

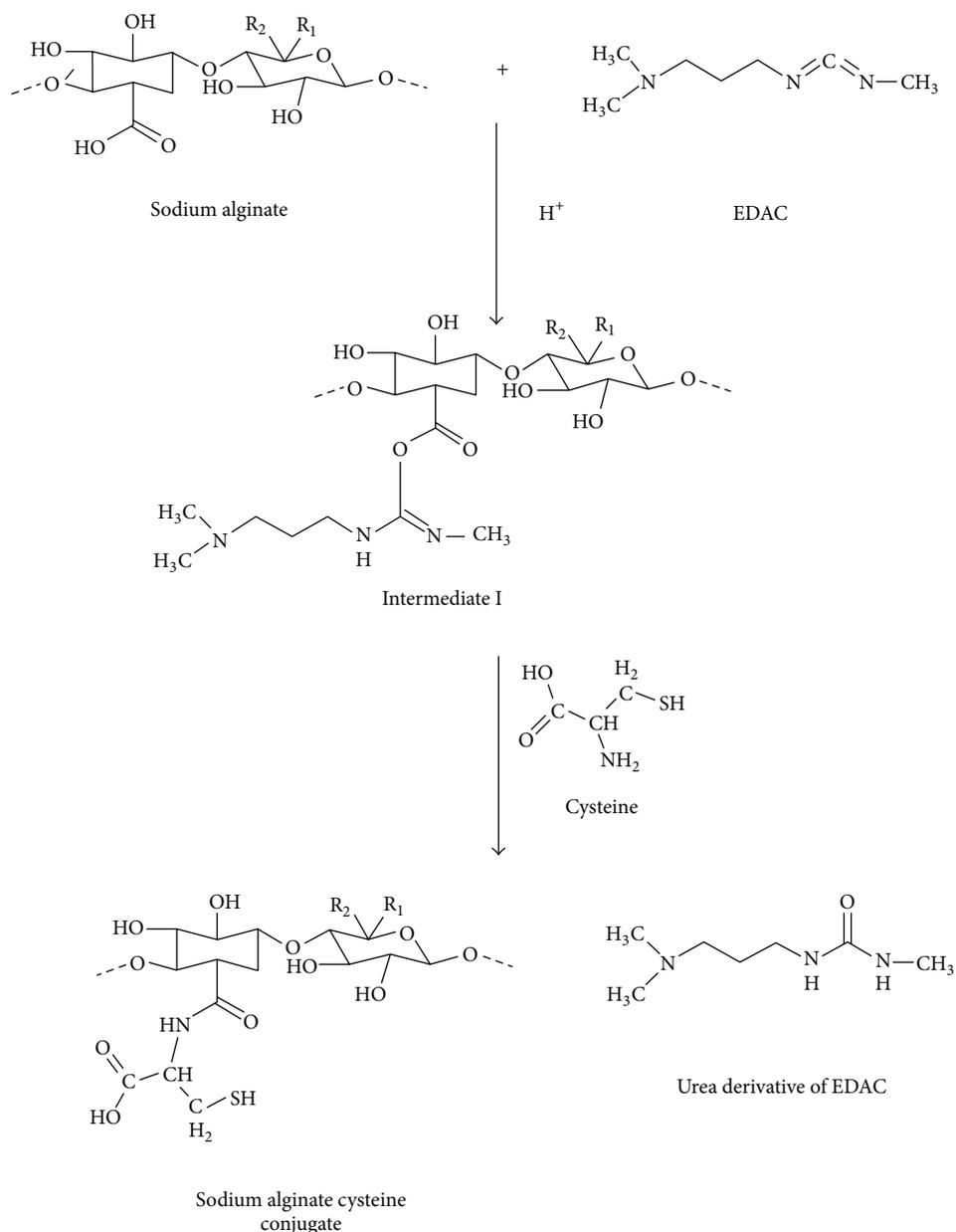


FIGURE 3: Process for thiolation of sodium alginate.

polyacrylic acid-cysteamine, CMC-cysteine, and alginate-cysteine (Table 1) [11].

**2.2.1. Sodium Alginate Cysteine Conjugate.** Sodium alginate is thiolated for surplus effects. In the presence of carbodiimide thiolation takes place (Figure 3) and the thiomers thus produced is studied and shown to have 50% more viscosity in comparison to the simple sodium alginate solution at 37°C. The swelling index is also improved [27]. Tablets thus prepared by using this modified polymer have shown to be more stable and resident on mucosa [28].

**2.2.2. Polyacrylic Acid Cystamine Conjugate.** Polyacrylic acid cystamine conjugates are prepared in the presence of carbodiimides by hydrolyzing polyacrylic acid polymer in

demineralized water. Hydrolyzed polymer shows up its carboxylic acid group for S-S conjugation [29].

Polyacrylic acid homocysteine conjugates prepared in the presence of carbodiimide have shown to contain sulfur  $930 \mu\text{mol} \pm 83$  per gram of thiomers. Polyacrylic acid homocysteine has shown to have improved mucoadhesive characteristics as compared to unmodified polymer.

**2.2.3. Sodium Carboxy Methyl Starch (CMS) and Carboxy Methyl Guar Gum (CMG) [30].** Thiomers of CMS and CMG are prepared in the presence of carbodiimide by coupling reaction. Thiol groups in the form of cysteine are conjugated. Thereafter the mucoadhesive properties of both the polymers are studied which showed CMS to be less mucoadhesive than CMG. On the other hand the swellability of CMG is not

affected by cysteine immobilization. On the whole CMG has proven to be better candidate as release of drug from the matrix tablet is 1.5-fold compared to CMS.

**2.2.4. Thiolated Xyloglucan.** Xyloglucans are important glycans that are cellulose microfibrils obtained from the seeds of the dicots. It is thiolated and its thiolation can be determined by Ellman's reagent while mucoadhesive extent can be determined by in situ gelling of the modified polymer [5].

### 3. Properties of Thiomers

Hydrophilic properties of thiomers due to the thiol group make the polyacrylic acid and chitosan more mucoadhesive [11]. Other properties include cohesive properties, mucoadhesive properties, enzyme inhibition, and permeation enhancement [7].

### 4. Characterization of Thiomers [29]

Thiomers are tested and characterized for their stability and effectiveness by various methods such as.

**4.1. Determination of Thiol Group Content [12].** The thiol group content on the polymer was determined by iodometry according to given procedure. The amount of thiol group tells the degree of thiolation. Hydrating with demineralized water thiomers was taken in the iodine flask. The pH of the solution was adjusted by adding 1 M HCl and then standard solution of 0.1 N iodine was added and shook for 30 minutes. Excessive iodine was titrated with 0.1 N sodium thiosulphate solution. Sarch is used as an indicator.

Same procedure mentioned above is used for estimation of blank without thiomers. The degree of thiolation is determined by following formula:

$$\begin{aligned} &\% \text{Thiol group content} \\ &= \frac{[(\text{Blank} - \text{Proper}) \times 0.1 \times 0.066 \times 100]}{0.1} \quad (1) \\ &\quad \times \text{weight of thiomers.} \end{aligned}$$

**4.2. Disulfide Bond Formation [12].** 200 mg of thiomers is hydrated with iodine in a flask and pH was adjusted between 2 and 3 using 1 M HCl. Then 0.6 mL of 3% solution of sodium borohydride was added to the polymer and shaken for 15 min to hydrate all the disulfide bonds to free thiol groups. After this the mixture is neutralized by addition of 0.5 mL of 1 M HCl. The thiomers before reduction and after reduction of thiol groups is subtracted to estimate disulfide content [31]:

$$\begin{aligned} &\% \text{Disulfide group content} \\ &= \frac{[(B_1 - B_2) \times 0.1 \times 0.066 \times 100]}{0.1} \quad (2) \\ &\quad \times \text{weight of thiomers,} \end{aligned}$$

where,  $B_1$  = Blank, burette reading after reduction;  $B_2$  = Blank, burette reading before reduction.

**4.3. Swelling Behavior [12].** Thiomers prepared at different pH are compared. 30 mg of thiomers was compressed into a disc of 5 mm diameter and dipped in demineralized water at 20°C by placing at permeable bottom tubes.

**4.4. Viscosity [12].** The viscometer is used to measure the viscosity of thiomers. 2% solution is prepared and temperature conditions of  $25 \pm 1$  were used at 20 rpm.

**4.5. Extent of Mucoadhesion: In Vivo.** The freshly excised intestinal mucosa of the sheep was taken to study the extent to which thiomers binds to the mucosa. The mucosa was clamped upside down and the exposed area was about 0.785 cm<sup>2</sup>. Equal amounts of all formulations are used to equilibrate each part. Every sample mucosa was exposed for 2 minutes with formulation to ensure the intimate contact between the two. The weights are used to detach the mucosa clamped in the pan to another; the weights thus used to detach mucosa are expressed as detachment stress which will be used to estimate in vivo mucoadhesion of thiomers in dynes/cm<sup>2</sup>. Consider

$$\text{detachment stress (dynes/cm}^2\text{)} = m * \frac{g}{A}, \quad (3)$$

where  $m$  is mass,  $g$  is acceleration due to gravity, and  $A$  is area of tissue exposed.

### 5. Routes of Drug Administration Using Thiomers as a Carrier of the Drugs

There are various routes of drug administration that can be used to deliver the drug using thiomers as carrier. They have various applications using these routes of administration. The thiomers preparations are available for oral, nasal, ocular, buccal delivery of the drug. In literature, it is studied that thiomers can be used to deliver the drug through transmucosal route, gastrointestinal route, buccal route, oral route, nasal route, ophthalmic route, and vaginal route of drug delivery. Different routes of drug administration along with the drugs that can be used through these routes are discussed as follows.

**5.1. Oral Delivery of Drug.** Oral route of drug administration is considered as safe and effective for various drugs. Effects of various drugs can be enhanced when they are administered through oral route using thiolated polymers such as increased stay of drug in intestine and prolonged contact, enhanced permeation, and enzyme inhibition [32]. Bioavailability of poorly bioavailable drugs like calcitonin, insulin, and low molecular weight heparin can be increased using thiomers based formulations. There are various applications of thiolated polymers in enhancement of bioavailability of poorly bioavailable drugs through oral route for example.

Calcitonin: calcitonin bioavailability is improved by conjugating it with the chitosan in modified form as compared to simple one due to the enzyme inhibiting and permeation enhancement effect [33]. It led to 5% more decrease in the calcium level [9].

**Insulin:** bioavailability and effect of insulin can be enhanced using thiolated polymer as the carrier in the form of matrix tablets. Thiolated polycarbophil using cysteine was used to carry the insulin in the form of tablets. This formulation showed 36% more decrease in the blood sugar level comparatively [9].

**Low molecular weight heparin:** low molecular weight heparin is administered subcutaneously which is painful and noncompliant; thus there is a need for the development of the oral drug delivery system which will provide improved bioavailability. Thiolated poly acrylic acid was used as a carrier to deliver the LMW heparin orally. It was observed that formulating low molecular weight heparin with thiolated polymers has shown to provide relatively improved bioavailability ( $5.8 \pm 1.4\%$ ) [9]. LMW heparin has shown absolute bioavailability of  $\geq 20\%$  in rats [34].

**5.2. Transmucosal Delivery of Drug.** Thiomers have the potential to deliver the drugs through transmucosal routes comparatively with better effects. Thiomers have the ability to provide the control drug release. In a study thiolated chitosan was prepared using thio butyl amidine as a conjugating agent. Chitosan thio-butyl-amidine microspheres were prepared to evaluate the controlled delivery of the active pharmaceutical ingredients. The results have showed the controlled release of drug through these microspheres. Thus thiomers can be effectively used for the less absorbed drugs to be delivered through mucosa [35, 36]. It is also concluded that the thiolated chitosan can be a good candidate for the formulation as beads for the controlled release of the drug [17].

**5.3. Gastrointestinal Delivery of Drug.** The recent advance in the polymer technology has led to improving in the drug delivery. The hydrophilic macromolecular drugs now can be effectively delivered using thiomers due to increased contact time by mucoadhesion and also due to enzyme inhibiting properties of thiomers as in case of GI peptidase [37].

Peptides: peptide delivery can be enhanced by incorporating it with thiomers. The oxidation of peptide is reduced and also the permeation of drug through the gut is increased due to increased stay of the formulation in the body. Thiolated chitosan can enhance the stability and dissolution profile of the orally delivered peptides. One of the formulations for the oral delivery of peptides is by using the thiolated chitosan and chitosan was thiolated as chitosan-thiol-butylamidine. It is compressed with tablets to deliver in gut. These tablets are coated with triglycerides to prevent adhesion in oral cavity or esophagus. In stated study enhanced bioavailability as well as stability was observed [30].

**5.4. Buccal Delivery of Drug.** Mucoadhesive buccal formulations are getting more and more attention. Thiolated polymers can be effectively used to enhance the buccal delivery of drugs especially the drugs with problems through trans-GIT delivery of the drugs. L-cysteine conjugates were used to prepare the matrix tablets and there after the unmodified and modified polymers used in preparation are further studies for effect on mucoadhesion. Thiomers thus prove to be an effective excipient for buccal delivery of the drugs [38].

**5.5. Nasal Delivery of Drug.** Thiomers can also be effective carrier for the delivery of drug through nasal route. Enhanced mucoadhesion and permeation make the thiomers effective tool for the delivery of drug through this route. Nasal route has been shown to be effective for delivery of drug using thiomers as permeation enhancement effect is more prominent. Various thiolated polymers including chitosan, sodium alginates, and polycarbophil can be used for the nasal delivery of the drug. Thiolated polycarbophil was used to study the leu-enkephalin delivery on the bovine mucosal cells. The results showed delivering the drug through the thiomers by sustained release and the degradation of drug is lowered. Also there was increase in drug uptake by nasal mucosa by 80-fold. Thus thiolated polycarbophil can prove to be a promising tool for nasal delivery drug [35].

Human growth hormone (hGH): thiolated polycarbophil and glutathione were used for the delivery of hGH through nasal route in the form of hydrogel. It was observed that this formulation has effectively improved the plasma level of the drug [9].

**5.6. Ophthalmic Delivery of Drug.** Ophthalmic drug delivery is an effective route of administration but it also has various drawbacks and the important one is decreased retention time of the drug. Various thiomers including thiolated chitosan, thiolated sodium alginate, thiolated poly ethylene glycol, and polycarbophil have the potential to deliver the drug effectively with increased mucoadhesion. A thiomers of nonionic surfactant; that is, cysteine-PEG was used to formulate the nanoparticulate preparation of the cyclosporine to deliver through the ophthalmic route and was shown to remain in the ocular cul-de-sac for about 6 h. Thus it has shown to increase the stay and also the concentration of drug in ocular region as compared to normal lipid carriers [39]. Similarly ocular inserts of using thiomers are carrier like thiolated polyacrylic acid that can also be formulated to improve the bioavailability as well as effectiveness of the drugs [35]. Various studies showed that plasmid DNA encoded with green fluorescence protein can be delivered with improved effects in a study; it was nanocomplexed with modified and unmodified chitosan to compare the effects of both carriers. Thereafter the transfection efficiency of thiolated chitosan and the sustained action produced by the thiolated chitosan was found greater comparatively [35, 40].

**5.7. Vaginal Delivery of Drug.** Delivery of drug through intravaginal route using thiomers offers various advantages like increased in situ gelling, controlled release, mucoadhesion, and enzyme inhibition thereby increasing the concentration of drug delivered. Thiomeric formulation to be administered through vaginal route can be in the form of tablets, capsules, gels, liquids, and so forth and once administered they remain there to deliver drug at a controlled release rate for even weeks [35].

In a study thiolated carbopol was used for vaginal delivery of LH-RH to observe the effect of thiomers on aminopeptidase N. it was observed that enzyme inhibition is greatly linked with thiol concentration. Increase in the concentration of thiol group improves the enzyme inhibition [41].

## 6. Conclusion

The improvement in the mucoadhesive properties of the polymers by incorporation of the thiol groups provides us with the polymers and ultimately the dosage form with multiple additive properties such as taste masking, improved permeation, prolonged release, reduced irritation, and patient compliance. Different polymers that are modified by addition of thiol groups are used in different preparations for different routes accordingly. By using these modified polymers the plasma drug levels are increased.

## Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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